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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,801	09/19/2001	Rajneesh Taneja	6842.US.01	1051

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,801	TANEJA ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

/Humera N. Sheikh/
HUMERA N. SHEIKH
PATENT EXAMINER
TC-1600

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response and Amendment after Non-Final Office Action and Applicant's Arguments/Remarks, all filed 09/16/05 is acknowledged.

Applicant has overcome the following rejection(s) by virtue of the amendment and/or persuasive remarks:

The 35 U.S.C. 102(b) rejection of claims 1, 2, 5, 6, 14, 15, 17 and 18 over the GB 747,293 reference.

The 35 U.S.C. §103(a) rejection of claims 1-21 over Phillips (USPN 5,840,737) in view of GB 747,293:

Claims 1-21 are pending in this action. Claims 1, 9 and 14 have been amended. Claims 1-21 remain rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 6 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Kouchiwa *et al.* (EP 0 264 259).

Kouchiwa *et al.* disclose stabilized, therapeutic pharmaceutical compositions comprising an active ingredient (dihydropyridines) in combination with one or more of *sodium carbonate*, sodium hydrogen carbonate, *calcium carbonate* and calcium hydrogen phosphate (see reference page 2, lines 1-32 and Abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over GB 747,293 in view of Chen *et al.* (U.S. Pat. No. 6,544,556 B1).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one pharmaceutical compound; and (b) a

pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

GB '293 patent teaches a pharmaceutical composition comprising a therapeutically effective amount of an acid-labile compound (erythromycin) in combination with acid neutralizers and buffers (see reference column 1, line 14 – col. 3, line 6).

Suitable, physiologically acceptable acid neutralizers disclosed are *aluminum hydroxide*, calcium hydroxide, sodium acetate, magnesium trisilicate, sodium phosphate, *calcium carbonate*, *sodium bicarbonate* and *sodium carbonate* (col. 2, lines 78-85). The acid neutralizers (buffers) may be used alone or in suitable combinations (col. 3, lines 4-6). The composition provides for adequate blood levels, whereby pH levels are effectively maintained.

The GB '293 patent teaches liquid suspensions. The '293 reference does not teach 'solid' formulations.

Chen *et al.* ('556) teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (see Abstract). The pharmaceutical compositions are preferably administered orally in oral dosage forms such as in the form of tablets, capsules, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, multiparticulate formulations, syrups, elixirs and the like (see column 4,lines 30-36); (col. 7, lines 22-30) and claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate oral, solid dosage forms, such as taught by Chen *et al.* within the liquid

formulations of the GB '293 patent. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Chen *et al.* teach that their oral dosage forms, which comprise proton pump inhibitors can be administered in effective and preferable dosage forms that include solid oral forms, such as tablets, granules or the like or alternatively in liquid oral forms such as suspensions or syrups to provide for the treatment of gastrointestinal side effects in a patient. The expected result would be improved, convenient solid dosage forms for the effective treatment of gastrointestinal disorders and conditions.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips (US Pat. No. 5,840,737) in view of GB 747,293 and further in view of Chen *et al.* (U.S. Pat. No. 6,544,556 B1).

The instant invention is drawn to a solid pharmaceutical formulation comprising: (a) a therapeutically effective amount of at least one pharmaceutical compound; and (b) a pharmaceutically acceptable protectant comprising (i) a water-soluble acid neutralizer; and (ii) a water-insoluble acid neutralizer.

Phillips ('737) teaches a pharmaceutical composition and methods for treating and/or preventing gastrointestinal conditions comprising active ingredients of acid-labile compounds (*i.e.*, omeprazole, lansoprazole and derivatives thereof) and a bicarbonate salt of a Group IA metal, preferably sodium bicarbonate (see reference column 7, line 3 – col. 8, line 46); Abstract & Claims.

The composition is used for the treatment of gastrointestinal conditions, including duodenal ulcers, gastric ulcers, gastroesophageal reflux disease (GERD), erosive esophagitis, and the like (col. 8, lines 47-61).

According to Phillips, the sodium bicarbonate acts as an antacid and protects the acid-labile compound (i.e., omeprazole) from acid degradation (col. 8, lines 34-37).

Phillips teaches a water-soluble acid neutralizer – sodium bicarbonate. Phillips does not teach a water-insoluble acid neutralizer, such as a carbonate or hydroxide.

The **GB '293** reference teaches a pharmaceutical, therapeutic composition, based on an acid-labile compound (erythromycin) wherein the composition comprises both water-soluble and water-insoluble acid neutralizers or buffers. Suitable acid neutralizers taught include, for example, *aluminum hydroxide*, calcium hydroxide, sodium acetate, magnesium trisilicate, sodium phosphate, *calcium carbonate*, *sodium bicarbonate* and *sodium carbonate* (col. 2, lines 78-85). The composition provides for adequate blood levels, whereby pH levels are effectively maintained through the use of the acid neutralizers.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the water-soluble and water-insoluble acid neutralizers taught by the GB '293 reference into the acid-labile formulation of Phillips because the GB'293 explicitly teaches acid neutralizers, which function to maintain pH levels within the body and further teaches the employment of acid neutralizers or buffers (i.e., *aluminum hydroxide*, *calcium carbonate*, *sodium bicarbonate & sodium carbonate, etc.)* in acid labile formulations. Similarly, Phillips teaches acid labile formulations for gastric acid disorders that contain water-soluble acid

neutralizers (i.e., *sodium bicarbonate*), which function as an antacid that protects the acid labile active compound. The expected result would be an improved and stabilized therapeutically effective acid labile formulation that maintains gastric pH levels and prevents degradation of acid labile drugs, as similarly desired by Applicant.

The Phillips ('737) and GB ('293) references are discussed above. They do not teach 'solid' pharmaceutical formulations.

Chen *et al.* ('556) teaches pharmaceutical formulations comprising a non-steroidal anti-inflammatory drug (NSAID) and a proton pump inhibitor in an amount effective to inhibit gastrointestinal side effects (see Abstract). The pharmaceutical compositions are preferably administered orally in oral dosage forms such as in the form of tablets, capsules, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsions, multiparticulate formulations, syrups, elixirs and the like (see column 4,lines 30-36); (col. 7, lines 22-30) and claims.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate oral, solid dosage forms, such as taught by Chen *et al.* within the liquid formulations of Phillips ('737) or alternatively in the GB '293 patent. One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Chen *et al.* teach that their oral dosage forms, which comprise proton pump inhibitors can be administered in effective and preferable dosage forms that include solid oral forms, such as tablets, granules or the like or alternatively in liquid oral forms such as suspensions or syrups to provide for the

treatment of gastrointestinal side effects. The expected result would be enhanced, solid gastric acid-relieving dosage forms for the beneficial treatment of gastrointestinal disorders.

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure:

US Patent No. 4,786,505 (Lovgren *et al.*) 11-1988

Response to Arguments

Applicant's arguments filed 09/16/05 have been fully considered.

35 U.S.C. §102(b) rejection over GB 747,293 of claims 1, 2, 5, 6, 14, 15, 17 & 18:

Firstly, Applicant argued, "GB 747,293 discloses an oral suspension composition containing erythromycin, a buffer and a suspending agent. The claims as presently amended are directed to a solid formulation, not liquid suspensions as disclosed in GB 747,293. Furthermore, GB '293 does not disclose or suggest the use or importance of a combination of a water-soluble and a water-insoluble neutralizer as is presently claimed."

Applicant's arguments have been fully considered, and were found to be persuasive, by virtue of the amendment incorporating the term 'solid' pharmaceutical formulation. Accordingly, the 35 U.S.C. §102(b) rejection over GB 747,293 of claims 1, 2, 5, 6, 14, 15, 17 & 18 has been withdrawn. However, the claims have now been rejected over GB '293 in view of Chen et al. (USPN 6,544,556). It is the position of the Examiner that Applicants have not demonstrated any unexpected and/or unusual results through 'solid' dosage forms. The

secondary Chen reference teaches the equivalency of liquids and solids in pharmaceutical formulations. Since the secondary reference teaches the equivalency of the use of pharmaceutical and therapeutically effective solid and liquid formulations as well as Applicant's teaching in their own specification, page 3, line 26 and page 10, lines 14-26, there are no unexpected results obtained in the use of a 'solid' pharmaceutical formulation. The forms are art-recognized equivalents. Additionally, it is noted that generic claim 1 permits any pharmaceutical compound.

35 U.S.C. §102(b) rejection over Kouchiwa *et al.* (EP 0 264 259) of claims 1, 5, 6 & 17:

Applicant argued, "Kouchiwa et al. discloses a solid pharmaceutical composition containing a 1.4-dihydropyridine derivative and a stabilizer which is at least one of sodium carbonate, sodium hydrogen carbonate, calcium carbonate and calcium hydrogen phosphate. Kouchiwa et al. adds these stabilizers to improve the shelf life of their composition and are not concerned with protecting a pharmaceutical compound from gastric fluid degradation. The control of pH and other in vivo considerations are not factors addressed by Kouchiwa et al. Thus, the importance of using a combination of water-soluble and water-insoluble neutralizers is not taught."

Applicant's arguments have been fully considered, but were not found to be persuasive. Applicant's argument that Kouchiwa et al. adds these stabilizers to improve the shelf life of their composition and are not concerned with protecting a pharmaceutical compound from gastric fluid degradation" was not persuasive since Kouchiwa et al. employs the same ingredients

required by Applicant and thus, the ingredients taught by the prior art would impart the same properties and beneficial results as the ingredients presently claimed herein. Moreover, it is not necessary that the prior art recognize each and every property attributable to a particular component or ingredient, but merely that the prior art recognize and teach the same component in a similar field of endeavor to impart similar results is sufficient. It is expected that since Kouchiwa et al. employs the same ingredients (*i.e.*, stabilizer), similar results and properties would be imparted thereby. Applicant's argument that "the prior art fails to teach the importance of using a combination of water-soluble and water-insoluble neutralizers" has been considered, but was not persuasive since the motivation of the use of these ingredients has been discussed and shown in the previous Office Action, taught by the prior art. As noted above, it is not necessary that the art recognize each and every benefit that accrues from these teachings, since the ingredients are incorporated for their intended purposes. No significant distinction over the art has been observed.

35 U.S.C. §103(a) rejection over Phillips (USPN 5,840,737) in view of GB 747,293 for claims 1-21:

Applicant argued, "Phillips discloses an aqueous solution or suspension of omeprazole containing a bicarbonate. The combination of Phillips and GB '293 lead only to a liquid formulation and does not disclose or suggest the importance of a combination of a water-soluble and water-insoluble neutralizers in a solid formulation as is presently claimed."

Applicant's arguments have been fully considered and were found to be persuasive with regards to the lack of a 'solid' pharmaceutical formulation for the combination of the Phillips

and GB '293 references. Accordingly, the rejection of claims 1-21 over Phillips in view of GB '293 has been withdrawn. However, claims 1-21 have now been rejected over Phillips in view of GB '293, further in view of Chen (USPN 6,544,556). While Phillips and the GB '293 references do not explicitly teach 'solid' forms, the Chen '293 reference recognizes and teaches the equivalency of liquids and solids in pharmaceutical formulations. Since the secondary reference teaches the equivalency of the use of pharmaceutical and therapeutically effective solid and liquid formulations as well as Applicant's teaching in their own specification, page 3, line 26 and page 10, lines 14-26, there are no unexpected results obtained in the use of a 'solid' pharmaceutical formulation. The forms are art-recognized equivalents. With regard to the argument that "The combination of Phillips and GB '293 does not disclose or suggest the importance of a combination of a water-soluble and water-insoluble neutralizers in a solid formulation as is presently claimed", the Examiner points out that, as noted above, it is not necessary that the art recognize each and every benefit that accrues from these teachings, since the ingredients are incorporated for their intended purposes. The ingredients employed in the prior art are the same as those instantly employed by Applicants and therefore, it is expected that similar, beneficial results could be attained, using the ingredients of the art. No patentable distinction over the art has been observed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh Humera N. Sheikh

Patent Examiner TC-1600

Art Unit 1615

April 28, 2006

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